REMARKS

I. Support for the Amendments

Claims1-8 and 11 have been amended. In order to further prosecution in a timely manner, claims 9-10 and 12-14 have been cancelled without prejudice to their pursuit in an appropriate continuation or divisional application.

Support for amended claims 1-8 and 11 can be found in the original specification and claims. Additional support for amended claims 1-4 can be found, e.g., on page 14, lines 5-14; from page 15, line 3, to page 17, line 31; and in the Examples. Additional support for amended claim 8 can be found, e.g., on page 15, lines 20-26; from page 15, line 3, to page 17, line 31; and in the Examples. Additional support for amended claim 11 can be found, e.g., from page 16, line 4, to page 17, line 31; from page 15, line 3, to page 17, line 31; and in the Examples. The amendments to claims 5-7 are a matter of form.

II. Status of the Claims

Claims 1-14 were originally in the application, with claim 1 being the independent claim. Claims 1-14 were subject to an Election/Restriction Requirement, and claims 1-8 and 11 (Group I) were elected with traverse.

In the Office Action mailed January 13, 2004, the Examiner rejoined claims 9-10, but stated that the restriction requirement remains in force for claims 12-14. The Examiner rejected claims 1-11, which were all the remaining claims.

Claims 1-11 were pending in the application, with claim 1 being the independent claim.

Claims 1-8 and 11 are presently in the application. Claims 1 and 11 are the independent claims. Claims 2-8 are now dependent on claim 1 or on a claim that is ultimately dependent on claim 1. In order to further prosecution in a timely manner, claims 9-10 and non-elected claims 12-14 have been cancelled without prejudice to their pursuit in an appropriate continuation or divisional application.

III. Acknowledgement of Foreign Priority Claim

The Examiner has acknowledged the claim for foreign priority and the receipt of all certified copies of priority documents. Applicants thank the Examiner for acknowledging the foreign priority claim and direct the Examiner's attention to the verified translation of the priority document, which was filed on February 28, 2002.

V. Remarks Concerning the Information Disclosure Statement

The Examiner has signed and initialed the PTO Form 1449 filed on June 21, 2001, but did not sign and initial the PTO Form 1449 filed on October 7, 2003. The Examiner states:

> The information disclosure statement filed 10/7/2002 fails to comply with 37 CFR 1.98(a)(2), which requires a legible copy of each U.S. and foreign patent; each publication or that portion which caused it to be listed; and all other information or that portion which caused it to be listed. It has been placed in the application file, but the information referred to therein has not been considered. If applicants wish the cited references to be considered, a new IDS comprising each reference must be submitted. (Pp. 2-3.)

Applicants respectfully submit, however, that the references and copy of the European Search Report were filed concurrently with this IDS (note Certificate of Mailing). As proof, Applicants submit a photocopy of the return postcard and note that the card was duly stamped by the U.S. Patent & Trademark Office and that the references and Search Report were not crossed off by the mailroom staff, thereby acknowledging that they were received. Applicants respectfully submit, therefore, that a new IDS is not necessary, although Applicants' representative agreed to re-submit the references during the telephone interview of January 23, 2004.

Therefore, Applicants submit herewith photocopies of the stamped postcard, the IDS, the PTO Form 1449, the references cited thereon, the European Search Report, and the Transmittal Letter (with Certificate of First Class Mailing dated October 2, 2002). Applicants respectfully request the Examiner to review and acknowledge the references accordingly. In accordance with the Examiner's instructions during the telephonic interview, Applicants note that no additional fee is due for this IDS, because it was submitted previously.

Applicants note that the Examiner did not initial reference BA (WO 98/31396; English language) cited in the IDS filed on June 21, 2001. Applicants respectfully request that the Examiner consider this reference in light of the discussion, *infra*.

VI. The Objections to the Drawings Have Been Accommodated

The Examiner has objected to the drawings as follows:

> New corrected drawings are required in this application because parts of the same sequence are presented in separate figures (i.e. SEQ ID NO: 1 has been

> presented as part of Figures 1-6). It would be remedial to amend the drawings to include SEQ ID NO: 1 as part of a single figure with multiple parts (i.e. parts A-F). In addition, applicants will need to amend the Brief Description of the Drawings to correspond to the amended drawings. (P. 3.)

Applicants have amended the drawings in accordance with the Examiner's request and submit corrected drawings herewith. Applicants have renumbered the figures accordingly and have amended the specification (particularly the Brief Description of the Drawings and the Examples) to correspond to the renumbered drawings.

Applicants respectfully submit that the corrections to the numbering of the drawings place the application in condition for allowance.

VII. Compliance with the Requirements for Sequence Listings

The Examiner alleges that the application is not in compliance with the requirements for sequence listings:

> This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825 because sequences were set forth that lack sequence identifiers and no computer readable format (CRF) was filed. These sequences include **the sequences present in the Figures (i.e. Figures 1-6) and the primer sequences in the working examples. Receipt is acknowledged of a paper filed 21 June 2001 in which a paper copy of the sequence listing, CRF and attorney's statement were filed. However, there is no record of a CRF in the file. It is necessary for applicants to submit a new CRF, paper copy and attorney's statement regarding similarity of the two and new matter.** If the Sequence Listing required for the instant application is identical to that of another application, a letter may be submitted requesting transfer of the previously filed sequence information to the instant application. For a sample letter requesting transfer of sequence information, refer to MPEP § 2422.05. Additionally, it is often convenient to identify sequences in figures by amending the Brief Description of the Drawings section (see MPEP § 2422.02).

> Applicants are required to comply with all of the requirements of 37 CFR 1.821 through 1.825. Any response to this office action that fails to meet all of these requirements will be considered non-responsive. The nature of the noncompliance with the requirements of 37 C.F.R. 1.821 through 1.825 did not preclude the continued examination of the application on the merits, the results of which are communicated below. (Pp. 3-4; all emphasis in original.)

Applicants respectfully submit that the electronic copy was duly filed with the application on June 21, 2001. As proof, Applicants submit a photocopy of the return postcard and note that the card was duly stamped by the U.S. Patent & Trademark Office and that the Computer Readable Sequence Disk was not crossed off by the mailroom staff, thereby acknowledging that it was received. As further proof, Applicants also submit a photocopy of the Notice of Acceptance of Application (mailed October 2, 2001), which lists the "Biochemical Sequence Diskette" as one of the items received by the U.S. Patent & Trademark Office. Applicants also submit copies of the Transmittal Letters (with Certificate of Express Mailing) filed June 21, 2001, along with a photocopy of the diskette mailer in which the diskette was mailed.

In accordance with the Examiner's instructions during the telephonic interview of January 23, 2004, Applicants submit herewith another paper copy of the sequence listing, another diskette, and another Statement. Applicants have also amended the application to include additional sequence identifiers. In accordance with the Examiner's instructions during the telephonic interview, Applicants note that no additional fee is due for this IDS, because it was submitted previously.

Applicants respectfully submit that the requirements for submission of a sequence listing have been met. Meanwhile, Applicants wish to thank the Examiner for proceeding to examine the application.

VIII. The Objection to the Specification is Accommodated

The Examiner has objected to the specification (pp. 4-5), because the Abstract consisted of multiple paragraphs and was greater than 150 words. Applicants have submitted a replacement abstract accordingly.

Applicants respectfully submit that the replacement Abstract places the application in condition for allowance.

IX. The Rejection of Claims 1-4 and 8-11 under 35 U.S.C. §101 is Partly Rendered Moot and Partly Accommodated

The Examiner has rejected claims 1-11 under 35 U.S.C. §101 (pp. 5-6). The Examiner alleges:

> Claims 1-4 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter.
>
> Each of the claims is directed to a DNA containing an uncoupling protein-2 (UCP-2) promoter region containing a regulator sequence. However, there is no indication in the claims that the "hand of man" is present in the claimed invention. Therefore, the claims improperly read on products of nature and are thus directed to non-statutory subject matter. It would be remedial to amend the claims to read "an isolated DNA".
>
> Claims 8-10 are rejected under 35 U.S.C. 101 because the claimed recitation of a use, without setting forth any steps involved in the process, results in an improper definition of a process, i.e., results in a claim which is not a proper process claim under 35 U.S.C. 101. See for example *Ex parte Dunki*, 153 USPQ 678 (Bd.App. 1967) and *Clinical Products, Ltd v. Brenner*, 255 F. Supp. 131, 149 USPQ 475 (D.D.C. 1966).
>
> Claim 11 is rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter.
>
> Claim 11 is improperly directed to both a composition (i.e. a "kit") and a method (i.e. "characterized by the use of').

Applicants have added the phrase "an isolated DNA" to claims 1-4 in accordance with the Examiner's suggestions and have added additional language with respect to the regulator sequence.

Applicants have revised the language of claim 8 to set forth the steps of "measuring and comparing polypeptide expression" in response to the Examiner's suggestions, while eliminating the "use" language. (Claims 9 and 10 have been cancelled without prejudice.)

Applicants have amended the language of claim 11 to be directed to a kit and its components.

Applicants respectfully submit that the cancellation of claims 9-10 without prejudice renders moot the Examiner's rejection of these claims under 35 U.S.C. §101. Applicants also respectfully submit that the amendments to claims 1-4, 8, and 11 accommodate the Examiner's rejection of these claims under 35 U.S.C. §101, thereby placing these claims in condition for allowance.

X. The Rejection of Claims 1-11 under 35 U.S.C. §112, Second Paragraph is Partly Rendered Moot, Partly Traversed, and Partly Accommodated

The Examiner has rejected claims 1-11 under 35 U.S.C. §112, second paragraph (pp. 6-7). Applicants respectfully disagree. The Examiner alleges:

> Claims 1-11 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.
>
> There is no clear and positive prior antecedent basis for the term "the regulator sequence" in claims 1-3. As disclosed in the instant specification, the upstream regulatory region for the UCP-2 gene comprises multiple regulatory

> factor binding sites. Thus it is unclear which of these regulatory sequences, or the entire upstream sequence, is encompassed by the cited phrase.
>
> Claims 8-10 provide for the use of a transformant comprising a recombinant vector of the invention in order to screen test compounds for their ability to modulate the expression of operatively linked sequences, but, since the claim does not set forth any steps involved in the method/process, it is unclear what method/process applicant is intending to encompass. A claim is indefinite where it merely recites a use without any active, positive steps delimiting how this use is actually practiced.
>
> Claim 10 is vague and indefinite in that it is unclear whether the compound to be identified is to necessarily possess all of the activities recited in the claim or must only possess one of the activities. It would appear, based upon reading the specification, that it would be remedial to amend the claim to include proper Markush group language such that the claimed method identifies a compound that necessarily has one of the recited activities. (Pp. 6-7; emphasis in original.)

With respect to the antecedent basis for the term "the regulator sequence," the language of claim 1 presently reads as follows:

> 1 (currently amended). An isolated DNA containing uncoupling protein-2 (UCP-2) promoter region containing a regulator sequence, wherein the regulator sequence is at least any one of the sequences selected from the group consisting of:
>
> a. a sequence containing peroxisome proliferator response element (PPRE) presented by position 284 to 296 of SEQ ID NO: 1;
> b. a sequence containing CCAAT/enhancer binding protein (C/EBP) biding sequence presented by position 1316 to 1320, position 1364 to 1368, or position 1698 to 1692 of SEQ ID NO: 1;
> c. a sequence containing glucocorticoid response element (GRE) presented by position 753 to 758, position 1023 to 1030, or position 1450 to 1455 of SEQ ID NO: 1; and
> d. a sequence containing MyoD presented by position 1428 to 1437 of SEQ ID NO: 1.

In the current language, Applicants have indicated regulatory sequences defined in the claim. Therefore, it is clear which regulatory sequences are encompassed. Claims 2-7 and 11 are dependent on claim 1 or on a claim dependent on claim 1, and the same language applies to claims 2-7 and 11.

Claim 8 has been amended to set forth the active, positive steps of "measuring and comparing polypeptide expression," while eliminating the "use" language.

In order to further prosecution in a timely manner, claims 9-10 have been cancelled without prejudice to their pursuit in an appropriate continuation or divisional application.

Applicants respectfully submit that the cancellation of claims 9-10 without prejudice renders moot the Examiner's rejection of these claims under 35 U.S.C. §112, second paragraph. Applicants also respectfully submit that the present amendments to claims 1-8 and 11 accommodate the Examiner's rejection of these claims under 35 U.S.C. §112, second paragraph, thereby placing these claims in condition for allowance.

XI. The Rejection of Claims 8-11 Under 35 U.S.C. §112, First Paragraph, is Partly Rendered Moot, Partly Traversed, and Partly Accommodated

The Examiner has rejected claims 8-11 under 35 U.S.C. §112, first paragraph (pp. 7-8). Applicants respectfully disagree. The Examiner alleges:

> Claims 8-11 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.
>
> Enablement is considered in view of the Wands factors (MPEP 2164.01(A)). These include: nature of the invention, breadth of the claims, guidance of the specification, the existence of working examples, state of the art, predictability of the art and the amount of experimentation necessary. All of the Wands factors have been considered with regard to the instant claims, with the most relevant factors discussed below.
>
> *Nature of the invention:* The nature of the invention is complex, involving the use of a transformant comprising a human UCP-2 promoter region to identify compounds that, at a minimum modulate expression of an operatively linked coding sequence (e.g. the coding sequence for the human UCP-2 gene).

Breadth of the claims: The methods encompass embodiments wherein the compound affects thermal regulation of body temperature, treats obesity, depression, hyperlipemia and/or is antipyretic.

Guidance of the specification/ The existence of working examples: The specification characterizes an ~6 kb region upstream of the human UCP-2 gene. The specification teaches the UCP-2 gene is thought to play a role in human obesity.

No working examples are provided for testing any compound of any type to determine its effect on expression from the identified UCP-2 promoter in human cells. No significant guidance is provided by applicants with regard to the type of compounds that are likely to have an effect on the promoter of the UCP-2 gene in human cells.

State of the art/Predictability of the art: The prior art does not appear to teach any compounds that would reasonably be expected to have an effect on the UCP-2 promoter in human cells.

The amount of experimentation necessary: Applicants have merely provided an assay (e.g. reporter gene activity) for identifying compounds that may modulate UCP-2 promoter activity in human cells without providing any significant guidance with regard to the production of compounds that can be reasonably expected to exhibit such activity. Therefore, one would have to practice undue, unpredictable experimentation in a trial-and-error manner in order to identify, if possible, compounds having the recited activities. Nor is there any convincing correlation between the UCP-2 protein and the recited activities (e.g. diabetes, depression, hyperlipemia) such that identification of a compound that modulates UCP-2 expression would necessarily identify a modulator of these activities. (Pp. 7-8; italics in original.)

The present language of claim 8 reads as follows:

8 (currently amended). A method for screening a compound or its salt that promotes or inhibits UCP-2 promoter activity characterized by measuring and comparing polypeptide expression between the transformant desribed in claim 7 contacted to test compounds and the transformant lacking the UDP-2 promoter contacted to the test compounds.

Applicants respectfully submit that the present language of claim 8 fully complies with the enablement requirement and enables one skilled in the art to make and/or use the invention. The Examiner's attention is drawn to the specification, particularly the portion of the specification from page 15, line 3, to page 17, line 31, and to the Examples.

With respect to the Examiner's rejection of claim 8 based on the *Wands* factors, applicants additionally note that WO 98/31396, which was filed with the first IDS (filed June 21, 2001), describes the relationship between expression and/or activity of UCP-2 to diseases such as obesity and diabetes. Example VI (p. 37) describes an increase in UCP-2 expression by thiazolidinediones (specifically BRL 49653). Therefore, in view of the state of the art, it is possible for one of ordinary skill in the art to practice the present invention according to amended claim 8.

The language of claim 11 presently reads:

> 11 (currently amended). A kit for screening a compound or its salt that promotes or inhibits UCP-2 promoter activity, which consists of cell culture medium, cell differentiation medium, plasmid for measurement of UCP-2 promoter activity, host cell line and test compounds.

The Examiner's attention is drawn to the specification, particularly the portion of the specification from page 15, line 3, to page 17, line 31, and to the Examples. The Examiner does not provide an explanation for the rejection of claim 11, but it is believed that the present amendments to claim 11 likewise make it possible for one of ordinary skill in the art to practice the present invention according to amended claim 11.

In order to further prosecution in a timely manner, claims 9-10 have been cancelled without prejudice to their pursuit in an appropriate continuation or divisional application.

Applicants respectfully submit that the cancellation of claims 9-10 without prejudice renders moot the Examiner's rejection of these claims under 35 U.S.C. §112, first paragraph. Applicants also respectfully submit that the present amendments to claims 8 and 11 accommodate the Examiner's rejection of these claims under 35 U.S.C. §112, first paragraph, thereby placing these claims in condition for allowance.

XII. The Rejection of Claims 1-7 Under 35 U.S.C. §102(b) Is Traversed

The Examiner has rejected claims 1-7 under 35 U.S.C. §102(b) "as being anticipated by Amaral et al. (U.S. Patent No. 5,807,740 issued 9/15/1998) or Amaral et al. (U.S. Patent No. 5,849,514 issued 12/15/1998)." Applicants respectfully disagree.

The Examiner alleges:

> Both patents disclose DNA containing a promoter region which includes a USP-2 regulator sequence and has a nucleotide sequence that coincides with bases 1762 to 2280 of SEQ ID NO: 1 (e.g. a "part thereof as in claim 4). In particular, cells transformed with UCP-2 promoters operably linked to reporter genes are taught for use in drug screening assays (e.g. Abstract, columns 3-4).

Applicants respectfully disagree with the Examiner's comments and traverse the anticipation rejection.

As noted, *supra*, the present language of claim 1 reads as follows:

> 1 (currently amended). An isolated DNA containing uncoupling protein-2 (UCP-2) promoter region containing a regulator sequence, wherein the regulator sequence is at least any one of the sequences selected from the group consisting of:
>
> a. a sequence containing peroxisome proliferator response element (PPRE) presented by position 284 to 296 of SEQ ID NO: 1;
> b. a sequence containing CCAAT/enhancer binding protein (C/EBP) biding sequence presented by position 1316 to 1320, position 1364 to 1368, or position 1698 to 1692 of SEQ ID NO: 1;
> c. a sequence containing glucocorticoid response element (GRE) presented by position 753 to 758, position 1023 to 1030, or position 1450 to 1455 of SEQ ID NO: 1; and
> d. a sequence containing MyoD presented by position 1428 to 1437 of SEQ ID NO: 1.

Applicants respectfully submit that a rejection under §102(b) requires the reference to contain each and every element of the rejected claim.

The cited Amaral references contain no description or suggestion of the regulator sequences specified in the amended claims. Nor is the claimed invention of claim 1 rendered obvious by either of these references.

Claims 2-7 are dependent on claim 1 or on claims dependent on claim 1, and the same arguments likewise apply to these claims.

Accordingly, neither Amaral reference anticipates claims 1-7 of the present application.

Applicants respectfully submit that the present claims 1-7 fulfill the requirements of 35 U.S.C. §102(b) and request the Examiner's reconsideration of these claims accordingly.

XIII. Conclusion

It is believed that all outstanding rejections have been addressed by this submission and that all the claims are in condition for allowance. If discussion of any amendment or remark made herein would advance this important case to allowance, the Examiner is invited to call the undersigned as soon as convenient.

In view of the foregoing amendments and remarks, the present application is respectfully considered in condition for allowance. An early reconsideration and notice of allowance are earnestly solicited.

Applicants hereby request a one-month extension of time for the Amendment and accompanying materials. If an additional extension of time is required, Applicants hereby request the Examiner to consider this a conditional petition for an extension of time. Although it is not believed that any additional fee (in addition to the fee concurrently submitted) is required to consider this submission, the Commissioner is hereby authorized to charge our deposit account no. 04-1105 should any fee be deemed necessary.

Respectfully submitted,

Date: May 12, 2004

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